

Claims

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of at least one of

5 SEQ ID NO.: 2, SEQ ID NO.: 4 and SEQ ID NO.: 6

for use as a medicament.

2. An isolated polypeptide according to claim 1, wherein said amino acid sequence has at
10 least 80% sequence identity to SEQ ID NO.: 2, SEQ IN NO.: 4 and SEQ ID NO.: 6.

3. An isolated polypeptide according to claim 1 or 2, wherein said amino acid sequence is a sub-sequence of with a minimum length of 10 amino acids.

15 4. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:2.

5. A polypeptide according to claim 4, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:2.

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6. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:4.

7. A polypeptide according to claim 6, wherein said polypeptide consists of the amino acid
25 sequence shown in SEQ ID NO:4.

8. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:6.

30 9. A polypeptide according to claim 8, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:6.

10. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:2.

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11. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:4.

12. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:6.

13. An polypeptide to claim 1-12, wherein said amino acid is consistently up-regulated
5 after antibody selection-induced change from VSA_{UM} to VSA_{SM} expression.

14. An polypeptide according to claim 1-13, wherein said amino acid sequence is capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not to the CD36 receptor.

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15. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of at least one of

a) SEQ ID NO.: 1, SEQ ID NO.: 3 SEQ ID NO.: 5 and SEQ ID NO.; 7,

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for use as a medicament.

16. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO.: 1, SEQ ID NO.: 3 SEQ ID NO.: 5 or SEQ ID
20 NO.; 7.

17. A nucleic acid according to claim 15-16, wherein said nucleotide sequence is a sub-sequence of with a minimum length of 30 nucleotides.

25 18. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:1.

19. A nucleic acid according to claim 18, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:1.

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20. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:3.

21. A nucleic acid according to claim 20, wherein said nucleic acid consists of the
35 nucleotide sequence shown in SEQ ID NO:3.

22. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:5.

23. A nucleic acid according to claim 22, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:5.
24. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide
5 sequence shown in SEQ ID NO:7.
25. A nucleic acid according to claim 24, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:7.
- 10 26. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:1.
27. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:3.
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28. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:5.
29. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least
20 80% sequence identity to SEQ ID NO:7.
30. A nucleic acid sequence according to claim 15-29, wherein said sequence is consistently upregulated after antibody selection-induced change from VSA_{UM} to VSA_{SM} expression.
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31. A nucleic acid according to claim 15-30, wherein said nucleic acid sequence encodes a polypeptide which is capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not the CD36 receptor.
- 30 32. A recombinant vector comprising the nucleic acid defined in any of claims 15-31 operably linked to one or more control sequences for use as a medicament
33. A composition comprising a polypeptide according to any of claims 1-14 or a nucleic acid according to any of claims 15-31 and a pharmaceutically acceptable diluent, carrier or
35 adjuvant.
34. A composition according to claim 33, wherein said composition is an immunogenic composition.

35. A composition according to claim 34, wherein said composition induces an IgG/IgM antibody response.
36. An isolated antibody or isolated antiserum induced in response to one or more polypeptides as defined in any of claims 1-14 and/or to one or more nucleic acids as defined in any of claims 15-31.
37. An antibody according to claim 36, wherein said antibody is capable of binding to a molecule expressed on the surface of an intact erythrocyte infected by a parasite causing malaria.
38. An antibody according to claim 36, wherein said antibody is capable of recognising parasites selected *in vitro* for expression of VSA_{SM}.
39. An antibody according to claim 36, wherein said antibody is capable of binding to a molecule expressed on the surface of an intact erythrocyte infected by a parasite capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not the CD36 receptor.
40. A vaccine comprising at least one nucleic acid according to any of claims 15-31 or at least one vector according to claim 32, the vaccine effecting *in vivo* expression of at least one antigen by a subject, to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to malaria caused by *Plasmodium falciparum*.
41. Use of a polypeptide according to any of claims 1-14 for the manufacture of a composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.
42. Use of a polypeptide according to any of claims 1-14 for the manufacture of a vaccine for malaria prophylaxis.
43. Use of a polypeptide according to any of claims 1-12 for the manufacture of a composition for vaccination against malaria.
44. Use of a nucleic acid according to any of claims 15-31 for the manufacture of a composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.

45. Use of a nucleic acid according to any of claims 1-31 for the manufacture of a vaccine for malaria prophylaxis.
46. Use of a nucleic acid according to any of claims 15-31 for the manufacture of a
5 composition for vaccination against malaria.
47. Use of a recombinant vector according to claim 32 for the manufacture of a composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.
- 10 48. Use of a recombinant vector according to claim 32 for the manufacture of a vaccine for prophylactic treatment of severe malaria.
49. Use of a recombinant vector according to claim 32 for the manufacture of a
15 composition for vaccination against severe malaria.
50. Use according to any of claims 41-49, wherein said malaria is caused by *Plasmodium falciparum*.
- 20 51. A method for prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in an subject said method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-31 or a recombinant vector according to claim 32.
- 25 52. A method for the prophylactic treatment of severe malaria in an subject, said method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-31 or a recombinant vector according to claim 32.
- 30 53. A vaccination method against severe malaria in an subject, said vaccination method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-31 or a recombinant vector according to claim 32.
- 35 54. A vaccine comprising any of the polypeptides according to any of claims 1-14, the nucleic acids according to any of claims 15-31 or the recombinant vector according to claim 32, said vaccine characterised in that it induces an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by a parasites.

55. A vaccine comprising one or more B-cell and/or T-cell epitopes originating from any of the polypeptides according to any of claims 1-14, the nucleic acids according to any of claims 15-31 or the recombinant vector according to claim 32, said vaccine characterised
5 in that it induces an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by a parasites.

56. A DNA vaccine, which results in the expression of a polypeptide comprising one or
10 more B-cell and/or T cell epitopes from any of the polypeptide sequences according to claim 1-14, wherein said vaccine is capable of inducing an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by parasites.

15 57. A DNA vaccine comprising at least one nucleic acid sequences according 15-31, wherein said vaccine is capable of inducing an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by parasites.

20 58. An *in vitro* diagnostic method, said method comprising contacting a sample with a polypeptide according to any of claims 1-14 under conditions allowing an *in vitro* immunological reaction to occur between said polypeptide and the antibodies possibly present in said sample, and *in vitro* detect the antigen-antibody complexes possibly formed.

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59. An *in vitro* diagnostic method according to claim 58, wherein a disease-state profile for a tested subject is generated by determining the concentration or expression level in a sample of sequences as defined in any of claims 1-14 and/or 15-31.

30 60. An *in vitro* diagnostic kit comprising

a) a sequence as defined in any of claims 1-14 and/or 15-31

b) reagents for preparing a suitable medium for carrying out an immunological reaction between an antibody present in a sample of body fluid or tissue and said sequence; and

35 c) reagents allowing the detection of the antigen-antibody complexes formed, wherein said reagents may bear a radioactive or non-radioactive label.

61. A method for generating a vaccine against severe malaria comprising

- a) injecting a sequence according to any of claims 1-14 in a subject
 - b) enabling said subject to generate antibodies specifically recognising any of the polypeptide sequences according to claim 1-14
 - c) purify said antibodies
 - 5 d) selecting antibodies having cross-reactivity to parasites causing severe malaria
 - e) selecting antibodies having the ability to inhibit adhesion to endothelial cells.
62. A method for testing an inhibitor-molecule capable of inhibiting binding of any of the polypeptides according to claim 1-14 to a receptor expressed on endothelia cells
- 10 comprising
- a) *in vitro* cultures of endothelial cells
 - b) add potential inhibiting-molecule
 - c) add RBC infected with parasites, said iRBC expressing any of said polypeptide sequences on their surface of the RBC
 - 15 d) measure the binding of the iRCB with said endothelia cells by microscopy or other means of quantifying binding as for instance liquid scintillation spectrometry.